of the two may be very close to each other; in fact, the two are separated from each other only by the transversus perinei. It might be said, therefore, that just when a hernia is in the formative period it would be exceedingly difficult to differentiate the two. In their subsequent growth, however, they take on an entirely different direction and appear upon the surface in widely different locations, namely, in the posterior part of the labium in the pudendal hernia and upon the buttocks in the perineal; there should therefore be no difficulty in differentiating the two herniæ at a stage of full development.

7. *Treatment.* No case of pudendal hernia is on record as having been cured. Of the 11 recorded cases only 2 have been operated, namely, Cases IX and X, both by von Winckel. The case reported by me is therefore the third case in which an attempt at a radical cure has been made by operation. Attempts by means of vaginal or labial plastics must be followed by failures, as no opportunity is given to follow up the two cardial principles underlying the radical cure of every hernia, namely, high ligation of the sac and a closure of the internal hernial ring. I am of the opinion that in spite of the difficulties which may be encountered this can best be attained by approaching the seat of the trouble by the abdominal route. It is perfectly possible, though not yet demonstrated, that in the spontaneous pudendal herniæ there is a well-defined ring, with firm enough structures surrounding such ring, *i. e.*, the levator ani and its superior and inferior fascial layers, which could be utilized for a plastic, with a fair promise of success. In the traumatic cases, however, the outlook for a radical cure is very meager indeed, as has been proved by my case also, in spite of the novel procedure attempted.

STUDIES IN CHOLELITHIASIS.

II. THE CLINICAL RELATIONSHIPS OF THE CHOLESTERINEMIA TO THE PATHOLOGICAL PROCESS.

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This communication will deal with the relationship of the cholesterin content of the blood to diseased conditions of the bile passages, the vast majority of these being accompanied by stone formation.

The individual blood determinations will then be compared with anatomical conditions present, and when complicating factors are present their significance will be discussed and the proper interpretation indicated. Finally, the clinical value of these laboratory determinations in the making of any individual diagnosis will be discussed.

The patients upon whom these studies were carried out were derived from the surgical services of Doctors Lilienthal, Beer, Berg, Elsberg and Moschcowitz at the Mount Sinai Hospital, New York. We are indebted to all of these gentlemen for their coöperation in this work.

As indicated above, no case has been included in this series unless an accurate anatomical diagnosis, made either at operation or autopsy, was available. Wherever more than one cholesterin determination was made before operation the figures given in the tables indicates an average. These figures are expressed in terms of milligrams of cholesterin for each 100 c.c. of blood. The methods employed in making the quantitative chemical estimations were described in the introductory paper of this series.

The first table details in a general way the essential facts in all of the cases studied without any attempt having been made to correlate the findings with the pathological conditions. In all of the following tables the symbols indicating the degree of jaundice are to be interpreted as follows:

+ = subicteric tint.
++++ = very deep jaundice.
++ and +++ = intermediary degrees of jaundice.

TABLE I.

Case.	Cholesterinemia, mg. per cent.	Temperature, F.	Jaundice.
185	0.322	99.6	++++
267	0.125	101.2	
351	0.3075	100.0	
330	0.230	98.6	
202	0.2125	98.6	+
331	0.1925	101.6	
328	0.190	98.6	
184	0.2425	98.0	±
194	0.2725	102.6	
85	0.175	98.6	+
495	0.235	98.6	
143	0.200	98.6	
270	0.155	100.0	
240	0.170	100.4	
344	0.132	98.6	
302	0.125	100.4	
207	0.250	99.8	
265	0.200	99.8	
284	0.162	98.6	
260	0.209	99.0	
294	0.205	98.6	
106	0.2725	98.6	++

Case.	Cholesterinemia, mg. per cent.	Temperature, F.	Jaundice.
222	0.176	99.4	+
226	0.190	98.0	
276	0.220	99.2	
148	0.212	99.0	
254	0.242	98.8	
166	0.190	99.0	
228	0.1475	101.6	
190	0.205	99.6	
263	0.1675	98.6	
181	0.110	102.4	
177	0.220	99.2	
94	0.150		
159	0.2975	98.6	
312	0.125	99.4	
306	0.190	100.4	
244	0.163	99.0	
433	0.1725	99.0	+
132	0.200		
1	0.238	99.8	++
384	0.2075	98.6	
199	0.161	99.2	
162	0.235	...	++
501	0.130	99.0	
250	0.235	99.8	
225	0.420	100.0	+++
272	0.162	99.0	
169	0.155	100.8	
343	0.250	99.4	++++
165	0.227	99.8	++
268	0.212	99.6	−
264	0.200	99.4	
179	0.205	99.0	
151	0.215		
127	0.237	...	+
269	0.230	102.0	+
382	0.175	99.8	
473	0.1575	99.6	
119	0.2375	99.0	+
126	0.200	98.6	+
128	0.1625	98.6	
195	0.176	100.2	
"S"	0.348	98.6	
273	0.1675	99.2	
134	0.290	98.6	
172	0.155	99.8	+
147	0.212	100.0	+
178	0.2725	103.6	++++
149	0.1328	100.4	++

In the following series of tables the cholesterin content of the blood is compared with the anatomical conditions present. These represent all of the pathological conditions one meets during the course of clinical, operating-room and autopsy experience. In practically all of the cases the macroscopic diagnosis of the conditions present have been verified and amplified by histological examination. These pathological conditions are as follows:

1. Gall-bladders which show a practically normal histological structure and contain usually a thin light colored bile or more rarely a viscid darker bile. Stones also are present varying in

number and size. The gall-bladder contents are very frequently bacteriologically sterile.

2. Gall-bladders frequently dilated and showing a normal or only a slightly abnormal histological structure and containing a single stone more or less impacted in the neck of the gall-bladder or in the cystic duct. The contained bile is very thin and watery. the bacteriological examination of the gall-bladder contents frequently gives negative results.

3. Large distended gall-bladders with walls of a normal thickness or somewhat thinned out, showing histologically more or less atrophy especially of the mucous membrane. The contained stones are numerous but lie loosely in the large amount of thin bile. Stones may also be present in the hepatic or common bile ducts and the ducts themselves may also be of larger caliber than normal. It may or may not be possible to cultivate bacteria from either the contained bile or stones, or from both.

4. Gall-bladders in which infection has taken place, containing a thin pus or more rarely a thick creamy pus with stones. The walls are thickened and edematous and the mucous membrane is very frequently gangrenous. Abscesses may be present in the wall of the gall-bladder or between it and the liver bed, or more rarely in the substance of the liver a short distance away. The stones contained may be numerous, indicating that conditions correspond to groups 1 and 2, with an added infection, or only a single stone is present, indicating that a hydrops, as described in group 2, has become secondarily infected. In all of these the cystic duct usually becomes shut off. Stones may also be present in any of the ducts.

5. Gall-bladders which have shrunken to less than their normal size and whose walls show a chronic productive inflammation, frequently with areas in which a more recent inflammatory reaction has occurred. The amount of pericholecystitis varies from a minimum to excessive degrees, in which it seriously hampers the necessary cholecystectomy. The contents of the gall-bladder may consist only of stones or bile which may or may not be purulent, or both of these; or thick emulsions of cholesterin, containing fragmentary stones, are present, and in which numerous cholesterin crystals can be seen under the microscope. When the cystic duct is open and a probe can be passed into the hepatic and common ducts the condition represents the end-results of groups 1, 2 and 3; when the cystic duct has been obliterated the condition is the end-result of group 4. It rarely happens that the scarring and contracture has advanced so far that only a short stump represents the gall-bladder.

6. Gall-bladders corresponding to those in groups 1 and 3, and with which there is associated a swelling of the head of the pancreas. Acute hemorrhagic pancreatitis of the fulminating type is not included in this group.

7. Empyemata of the gall-bladder without stone formation.

These are pure infections, and bacteria can always be cultivated from the gall-bladder contents.

8. Gall-bladders corresponding in structure to group 5 but without stone formation. These represent the end-results of those in group 7.

The results of the quantitative chemical determinations of the cholesterin content of the blood in these groups are detailed as follows:

TABLE II.—PATHOLOGICAL GROUP 1.

Case No.				Mg., per cent.
Case No. 263,	cholesterin	blood content	=	0.167
94,	"	"	=	0.150
312,	"	"	=	0.125
172,	"	"	=	0.155

The cases grouped in Table II show normal figures for the cholesterin content of the blood.

TABLE III.—PATHOLOGICAL GROUP 2.

Case No.				Mg., per cent.
Case No. 207,	cholesterin	blood content	=	0.250
250,	"	"	=	0.235

TABLE IV.—PATHOLOGICAL GROUP 3.

Case No.				Mg., per cent.	
Case No. 331,	cholesterin	blood content	=	0.1925	
328,	"	"	=	0.190	
143,	"	"	=	0.200	
260,	"	"	=	0.209	
276,	"	"	=	0.220	
254,	"	"	=	0.242	
166,	"	"	=	0.190	
268,	"	"	=	0.212	
179,	"	"	=	0.205	
119,	"	"	=	0.237	(jaundiced)
134,	"	"	=	0.290	
147,	"	"	=	0.212	(jaundiced)
177,	"	"	=	0.220	
265,	"	"	=	0.200	
151,	"	"	=	0.215	

The cases grouped in Tables III and IV, corresponding to the pathological groups 2 and 3, are biologically of a similar order and therefore it is to be expected that the cholesterin content of the blood would show figures of approximately the same range. The figures are all high notwithstanding the fact that only two of all the patients in the series had obstruction in the common duct and were jaundiced.

TABLE V.—PATHOLOGICAL GROUP 4.

				Mg., per cent.	
Case No. 194,	cholesterin blood	content	=	0.2725	(in puerperium)
240,	"	"	=	0.170	
302,	"	"	=	0.125	
284,	"	"	=	0.1625	
148,	"	"	=	0.212	
228,	"	"	=	0.1475	
181,	"	"	=	0.110	
384,	"	"	=	0.207	(diabetic)
169,	"	"	=	0.155	
264,	"	"	=	0.200	(pregnant)
127,	"	"	=	0.237	(jaundiced)
382,	"	"	=	0.175	
128,	"	"	=	0.162	
195,	"	"	=	0.176	
178,	"	"	=	0.2725	(jaundiced)
149,	"	"	=	0.132	

This table represents the findings in pathological group 4. The cholesterin content of the blood in these cases shows a normal or subnormal range unless some complicating factor is present. The individual explanations for the hypercholesterinemia cases are as follows:

Case No. 194, patient in puerperal period.
No. 264, patient pregnant.
No. 127 and 178 had obstruction in the common duct.
No. 384, patient was a diabetic.
No. 148, we have no explanation for this last figure. Possibly some complicating factor had been overlooked or omitted from the clinical records.

TABLE VI.—PATHOLOGICAL GROUP 5.

				Mg., per cent.	
Case No. 185,	cholesterin blood	content	=	0.322	(jaundiced)
267,	"	"	=	0.125	
85,	"	"	=	0.175	
495,	"	"	=	0.235	
294,	"	"	=	0.205	
222,	"	"	=	0.176	
226,	"	"	=	0.190	
190,	"	"	=	0.205	(pregnant)
159,	"	"	=	0.297	
306,	"	"	=	0.190	(jaundiced)
199,	"	"	=	0.161	
162,	"	"	=	0.235	(jaundiced)
501,	"	"	=	0.130	
272,	"	"	=	0.162	
165,	"	"	=	0.227	(jaundiced)
269,	"	"	=	0.230	(jaundiced)
344,	"	"	=	0.132	
270,	"	"	=	0.155	
433,	"	"	=	0.1725	

Table VI gives the findings for the cases in group 5. The figures vary. A few are normal but most are high. Some of the high figures are so because of complicating factors. These are as follows:

Cases Nos. 162, 165, 185, and 269 are high because of obstruction in the common duct.
No. 306 is high because of common duct obstruction plus a nephritis.
No. 190 was pregnant at the time of observation.

TABLE VII.—PATHOLOGICAL GROUP 6.

		Mg., per cent.
Case No. 202, cholesterin blood content	=	0.212
132, " "	=	0.200
225, " "	=	0.420

The figures in Table VII are uniformly high.

TABLE VIII.—PATHOLOGICAL GROUP 7.

		Mg., per cent.	
Case No. 106, cholesterin blood content	=	0.272	(jaundiced)
343, " "	=	0.250	(jaundiced)
473, " "	=	0.157	

TABLE IX.—PATHOLOGICAL GROUP 8.

		Mg., per cent.	
Case No. 184, cholesterin blood content	=	0.2425	(jaundiced)
126, " "	=	0.200	(jaundiced)

In Tables VIII and IX are the figures for the cases in groups 7 and 8. They are usually normal unless some complicating factor is present. All of the high figures given are due to a coexisting common duct obstruction due to inflammatory swelling.

Discussion. Diseased conditions of the bile passages are very liable to become associated with or initiated by disturbances in the normal physiological processes of the cholesterin metabolism, and in accordance with the pathological activities are readily divided into two classes:

1. Those without gall-stone formation.
2. Those will gall-stone formation.

The diseased condition of the bile passages may have been initiated by a bacterial infection. It may remain a purely infective process or it may cause changes in the excreted bile, with subsequent stone formation; or, as pointed out in the first paper, there may be a primary disturbance in the cholesterin metabolism leading to a precipitation of stones and finding its inception most frequently during the physiological period of pregnancy. A quiescent period may then follow, and frequently this continues, with or without symptoms, for the remainder of that particular individual's life. Recrudescences may, however, occur, perhaps frequently repeated at irregular intervals, due either to repetitions of the physiological disturbances or to renewed or complicating infection, or to both, and occurring either independently at different times or simultaneously at the same time. In these metabolic disturbances the bile passages undergo changes either mechanically, owing to the presence of stones which act as foreign bodies or as a response to the added bacterial infection, or to the combination of these two acting together or alternately at different times.

At any given moment the state of the blood's content of cholesterin is influenced on both sides of the normal range by associated conditions of the body which may have nothing in common with the physiological processes of the cholesterin metabolism and the interpretation of any blood determination must take into account these complicating factors. These are as follows:

1. The cholesterin content of the blood is lowered:

(*a*) By a diet which is poor in lipoids.

(*b*) By the occurrence of high temperatures.

2. The cholesterin content of the blood is increased.

(*a*) By a diet excessively rich in lipoids.

(*b*) By the presence of other diseased conditions especially atherosclerosis, diabetes and nephritis.

(*c*) During pregnancy. The hypercholesterinemia of pregnancy usually lasts for a variable period after evacuation of the uterus.

(*d*) By the presence of obstruction in the common bile duct. If the obstruction, however, is not absolute, as indicated by the degree of the accompanying jaundice, the cholesterin content of the blood may not be increased. This is illustrated in Table X.

TABLE X.

	Mg., per cent.		Temperature F.
Case No. 185, cholesterin =	0.322	(jaundice) ++++	99.6
202, " =	0.2125	+	98.6
184, " =	0.2425	+	98.0
106, " =	0.2725	++	98.6
222, " =	0.176	+	99.4
244, " =	0.163	+	99.0
1, " =	0.238	++	99.8
162, " =	0.235	++	100.0
225, " =	0.420	+++	100.0
343, " =	0.256	++++	99.4
165, " =	0.227	++	99.8
127, " =	0.237	+	
269, " =	0.230	+	102.0
119, " =	0.2375	+	
126, " =	0.200	+	98.6
172, " =	0.155	+	99.8
147, " =	0.212	+	100.0
178, " =	0.272	++++	103.6
149, " =	0.132	++	100.4

In the classifications given in the first half of this paper the individual tables seem to show a uniformity in the cholesterin contents of the blood for each group of cases, when all of the complicating factors detailed above are properly taken into account. The only apparent discrepancies would be found in the cases grouped in Table VI (pathological group 5). The explanation of these apparent discrepancies lies in the natural history of these disturbances.

During our studies it has become increasingly evident that the subdivisions into groups attempted above is artificial and that these groups form a continuous progression. This has already been hinted at in describing these groups. The biological sequence of events may be one of three:

1. The pure infections illustrated best in groups 7 and 8 (Tables VIII and IX). The element of the cholesterin metabolism does not enter unless there is a complicating obstruction in the common bile duct. Only in that contingency does the cholesterin content of the blood range high. The complicating obstruction is due to swelling in the duct or to inflammatory swelling or adhesions about the duct. The affection begins as an empyema of the gall-bladder, and when repeated recrudescences of infection are permitted it terminates in the contracted and shrunken gall-bladder of group 8 (Table IX).

2. The cases that have their origin in disturbances in the cholesterin metabolism. Most often these disturbances in function are initiated by the physiological changes which accompany pregnancy. The hypercholesterinemia of pregnancy may reach such a degree that the accompanying supersaturation of blood and bile is rectified to the normal by a precipitation of stones in some portion of the bile passages, almost always the gall-bladder. This immediately furnishes the explanation for the patients with normal gall-bladders containing stones, the cholesterin contents of whose bloods are normal. At some time previous to the observation there had occurred a hypercholesterinemia which had been restored to the normal by a precipitation of stones. No further hypercholesterinemic crisis having occurred, these patients have had symptoms due to the mechanical effects of the stones acting as foreign bodies and have submitted themselves to operation at this stage. It is to be expected that the cholesterin content of the blood of such patients would be normal at the time of operation.

The original factor which had caused the hypercholesterinemia may continue, however, or may be repeated at intervals, so that at the time of observation the cholesterin content of the blood is relatively high. These are conditions exemplified in group 2 (Table III) and to a large extent in group 3 (Table IV).

3. Combinations of infection and disturbed cholesterin metabolism may occur either simultaneously or alternately and with different degrees of intensity. Depending on the factor which is paramount, or the stage of the process, or the presence or absence of complicating factors, which now become numerous, the cholesterin content of the blood is found to be below the normal, at the normal or much above the normal range. These cases are illustrated in groups 2, 3, 4 and 5 (Tables III, IV, V and VI).

The apparent discrepancies in the figures given in Table VI (group 5) are now explainable. This group represents the end-results of several other groups and the cholesterin content of the blood is found to vary as these do.

From the foregoing facts it must be conceded that in any given case the diagnostic value of any determination of the cholesterin content of the blood is a variable and dubious one. One can summarize those gall-bladder conditions in which the cholesterin content of the blood is normal as follows:

1. In the presence of stones in a normal gall-bladder, without common duct obstruction and with or without high temperatures.
2. In the presence of a chronically inflamed gall-bladder containing stones without common duct obstruction and with or without high temperatures.
3. In the presence of any of the above with incomplete obstruction of the common bile duct.
4. In the presence of an empyema of the gall-bladder, with or without stones, with low or high temperatures and with no obstruction in the common duct.
5. In conditions as in the preceding division (4), with partial or complete obstruction of the common duct.

The finding of a hypercholesterinemic condition, while usually pointing to some disturbance in the cholesterin metabolism and in the bile passages, is always subject to correction in the presence of any of those complicating factors, mentioned in the early part of this discussion, which, by themselves, are capable of increasing the cholesterin content of the blood. And when this correction is to be made it becomes difficult, if not impossible, to decide whether the entire excess of the cholesterin in the blood above the normal is due wholly or only in part to these complicating factors. The situation becomes all the more complex when it is known that it is possible to obtain hypercholesterinemic figures in other diseased conditions, some of which are herewith illustrated:

TABLE XI.

Case No.	Cholesterinemia, Mg., per cent.	Diagnosis.	Temperature, F.
224	0.190	Neurosis	98.6
243	0.265	Diabetes	98.0
369	0.200	Tuberculosis	100.2
317	0.2625	Carcinoma of liver	102.0
534	0.220	Colloid goiter	99.0
215	0.200	Nephritis	98.6
214	0.190	Nephritis	98.6
283	0.205	Phlebitis of leg	
"S"	0.325	Carcinoma of stomach	98.6
"R"	0.200	Sepsis	100.4
"TR"	0.250	Gastric ulcer	
"SW"	0.220	Chronic appendicitis	

The occurrence of a hypercholesterinemia can be used as a diagnostic factor in only one circumstance. When a distinction must be made between the jaundice due to cirrhosis of the liver and the jaundice due to common duct obstruction the finding of a hypercholesterinemic condition indicates that obstruction is present. Cirrhotic conditions uniformly give low figures for the cholesterin content of the blood.

Such a state of affairs goes to show that with gall-bladder conditions the proper interpretation of any cholesterin determination is only possible after a knowledge is obtained of the actual anatomical conditions. Only then is one enabled to reason backward and deduce the natural history of the actual pathological disturbance which underlies the entire disease. Such knowledge will then furnish scientifically correct and adequate data upon which a rational method of treatment may be based.